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09/844,815	04/30/2001	Gary E. Rehm	MSE #2610	3326

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COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/844,815	Applicant(s) REHM ET AL.	
	Examiner Gary W. Counts	Art Unit 1641	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-16* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the claims

The amendment filed May 15, 2003 is acknowledged and has been entered. Claims 1-7 and 9-16 remain pending in the application. Claims 11-14 have been withdrawn from consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-7 and 9, 10, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 10, lines 14-19 in the specification. Applicant discloses "Phosphate and carboxyl groups are common as the charged ionizable groups of buffering agents and calcium salts of these groups are not very water soluble (calcium phosphate is relatively insoluble), so they tend to precipitate from solution." The applicant does not disclose that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic chelating agent. There is no description in the specification disclosing that the buffered assay

medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic chelating agent.

2. Claims 1-7, 9, 10, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 10, lines 14-19. Applicant discloses "phosphate and carboxyl groups are common as the charged ionizable groups of buffering agents and calcium salts of these groups are not very water soluble (calcium phosphate is relatively insoluble, so they tend to precipitate from solution." The applicant does not specifically disclose a calcium free buffer. On page 17 lines 10-20. Applicant discloses strip development using phosphate buffer and Tris to improve the buffering capacity of the strip. The applicant does not disclose a calcium free buffer.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7, 9, 10, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because part (iii) of the claim recites a calcium free buffer and further goes on to recite calcium present in the buffered assay medium. It is unclear how it is a calcium free buffer if it contains calcium.

Claim 1, lines 9 and 10 "in sufficient quantity" is vague and indefinite. It is unclear what is considered to be a sufficient quantity because there is no definition or guidance provided for the phrase in the specification.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4, 7, 9, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al (US 5,856,117) in view of Berry et al (US 5,384,247).

Uenoyama et al disclose a method for measuring the concentration of urinary trypsin inhibitors which involves mixing a urine sample, trypsin, and a buffer solution and the addition of a substrate solution to cause the enzyme reaction, and measuring the activity of trypsin (col 5, lines 39-60). Uenoyama et al also teach the use of dimethylfomamide as the solvent (col 6, line 11) and a buffered pH of 7.8 (col 7, line 46) and the substrate present in a concentration of 1 to 50 mmol/l (col 4, line 16) and trypsin in the concentration of 10 to 500 mg/l preferably 20 to 100 mg/l (col 5, line 52). Uenoyama et al also disclose that the buffer solution can be a Tris buffer or phosphate buffer (col 6, lines 46-48).

The method of Uenoyama et al differs from the instant invention in failing to disclose the use of a polycarboxylic chelating agent to inhibit interference of calcium present in the urine.

Berry et al (US Patent 5,384,247) teach the use of EGTA and EDTA as chelating agents which inhibit the interfering ions of calcium in a urine sample (col 4, line 53 - col 6, line 17) (claims 27 and 34). The use of these chelating agents reduce the free concentration of interfering ions to levels where interference is no longer significant and increase the sensitivity of the enzyme to an analyte with respect to the interfering ion (col. 3, lines 45-52).

It would have been obvious to one of ordinary skill in the art to incorporate the polycarboxylic chelating agents of Berry et al into the method of Uenoyama et al because Berry et al shows that the use of these chelating agents provide the advantage of reducing the free concentration of interfering ions to levels where interference is no longer significant and also increase the sensitivity of the enzyme to an analyte.

With respect to the specific concentration of the chelating agents recited in the instant claims, the optimum concentration of chelating agent can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art.

With respect to a calcium free buffer as recited in the instant claims. Because the claim recites a calcium free buffer and then recites calcium present in the buffered assay medium. Examiner interprets this to mean that a calcium free buffer can contain calcium. Therefore the Uenoyama et al teaches reads on this limitation because their buffer contains calcium.

7. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al in view of Berry et al as applied to claims 1-4, 7, 9, 15 and 16 above, and further in view of May et al (GB 2,204,398 A).

See above for teachings of Uenoyama et al and Berry et al.

Uenoyama et al and Berry et al differ from the instant invention failing to disclose dry test reagents and a dry test device which the urine test sample can flow by dipping the dry test device into the buffered assay medium.

May et al disclose a device comprising a hollow casing constructed of moisture-impervious solid material containing a dry porous carrier which communicates indirectly with the exterior of the casing, a sample receiving member protrudes from the casing such that a liquid test sample can be applied to the receiving member and permeate to the porous carrier which contains impregnated reagents (page 15, lines 16-35 and page 16, lines 1-9). This diagnostic test device allows for quick and convenient use and requires the user to perform as few actions as possible (page 2, lines 29-35).

It would have been obvious to one of ordinary skill in the art to use the device of May et al to practice the method of Uenoyama et al as modified by Berry et al, because May et al shows that the device allows for quick and convenient use and requires the user to perform as few actions as possible, where all the necessary reagents are all present on a single solid support.

8. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al in view of Berry et al as applied to claims 1-4, 7, 9, 15 and 16 above, and further in view of Nanbu et al (US 6,130,055).

See above for teachings of Uenoyama et al and Berry et al.

Uenoyama et al differ from the instant invention in failing to disclose arginine or lysine derivatives as the substrate for trypsin.

Nanbu et al discloses a method for measuring the concentration or activity of urinary trypsin inhibitor. Nanbu et al teach mixing a sample, trypsin solution, and a substrate in a solution and measuring the tryspin activity. Nanbu et al also teach that this substrate may come from the amino acid residues of the L-type (col 2, lines 13-23). The use of this substrate would allow for excellent solubility.

It would have been obvious to one of ordinary skill in the art to incorporate the trypsin substrates of Nanbu et al into the method of Uenoyama et al as modified by Berry et al because Nanbu et al shows that the use of the L-type amino acid residues allows for excellent solubility (col 2, line 23).

Response to Arguments

Applicant's arguments filed May 15, 2003 have been fully considered but they are not persuasive.

112 first paragraph argument

Applicant argues that the specification does disclose that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with polycarboxylic chelating agent. Applicant specifically directs attention to page 2 lines 28-31, Summary of the Invention, disclosing "a polycarboxylic chelating agent in sufficient quantity to inhibit interference with the assay from calcium present in the urine test sample." This is not found

persuasive because this polycarboxylic chelating agent is for inhibiting interference of calcium present in the urine sample. The disclosure does not state that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with polycarboxylic chelating agent. Applicant further states that the specification also teaches that the "assay of the present invention is based on the discovery that the interference with the urine trypsin assay caused by the presence of calcium ion in the urine can be factored out of the assay by the use of certain chelating agents." Specification page 4,lines 21-30. Applicant states that in Example 1, the specification discloses that the "maximum practical amount of calcium in urine was determined to be 80 mg/dl based on published data and double the amount of EGTA (polycarboxylic chelating agent) (0.47 g/L to complex this amount of calcium was added to the assay system." Specification, page 7, lines 15-19. Later in Example 1, after comparing samples containing polycarboxylic chelating agents with those lacking polycarboxylic chelating agents, it "was further determined that the calcium either had to be overwhelmed of complexed to remove it from the assay system. This is not found persuasive because the Applicant has not disclosed that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with polycarboxylic chelating agent, but rather discloses that the polycarboxylic chelating agent is in sufficient quantity to inhibit interference with the assay from calcium present in the urine test sample. All instances in which Applicant directs attention to are focused on overwhelming or removing calcium present in the urine test sample. The

disclosure or none of the examples state that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with polycarboxylic chelating agent.

112 second paragraph argument

Applicant argues that the amendment to claim 1 to supplement the term "in sufficient quantity" by inserting a definite numerical concentration range for polycarboxylic chelating agent renders the rejection moot. This is not found persuasive because Applicant has not recited the concentration of calcium present in the buffered assay medium and it is unclear what is considered to be a sufficient quantity of calcium to not interfere with the binding of calcium present in the urine test sample. Furthermore, there is no guidance in the specification provided to ascertain what would be considered sufficient.

103 rejection arguments

Applicant argues that the amendments to the claims distinguish the instant claims from Uenoyama. Specifically, Applicant focuses on the new limitation "a calcium free buffer" and states that the term "calcium free buffer" is well known in the art to refer to buffers have low levels of free calcium ions. This is not found persuasive because Applicant has not provided evidence that the term "calcium free buffer" is well known in the art. Further, Applicant has not disclosed what is considered to be a low level of calcium present in the buffered assay medium.

Applicant argues that guidance as to what a "sufficient quantity" of calcium would be to interfere with the chelating agent is found in the specification. "The maximum

practical amount of calcium in urine, was determined to be about 80 mg/dl based on published data and double the amount of EGTA (0.47) needed to complex this amount of calcium was added to the assay system." Specification at page 7, lines 15-19. This is not found persuasive because the disclosure does not state what is considered to be a low level of calcium present in the buffered assay medium.

Applicant argues that the amended claims are distinguished from the Uenoyama reference, in which the buffer solution contains "at least 0.15 umol per 1 ug of protease". And that Uenoyama uses a TEA buffer containing dissolved calcium salt (col 7, lines 50-51). Applicant further argues that the calcium free buffers in the claimed assay either remove calcium from the assay medium or else contain a low level of free calcium ions that there is no interference with the binding of calcium present in the urine test sample to the polycarboxylic chelating agent. This is not found persuasive because it is unclear what a calcium free buffer is because Applicant has not provided support or guidance for a calcium free buffer or any evidence that the term is well known in the art. It is also unclear because the claim recites a calcium free buffer then recites that the buffer contains calcium. Further, it is noted that Uenoyama et al uses a TEA buffer. However, Uenoyama et al specifically teaches that the buffer solution can be a Tris buffer or phosphate buffer (col 6, lines 46-48) (the same buffers as recited in claims 15 and 16). As stated above the instant claims incorporate an amount of calcium and since it is unclear how much calcium is present in the instant claims and since Uenoyama et al teach the same buffers as the instantly recited claims it is the Examiner's position that the Uenoyama et al reference still reads on the instant claims.

In response to applicant's argument that the Berry reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., does not "mask" calcium, and EGTA reduces variation between urine samples having increasing amounts of calcium) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
July 9, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
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07/21/03